Exhibit C

Example 11: Effect of PYY **in vivo**

The Zucker Diabetic Fatty (ZDF) male rat is a recently developed inbred (> F30 Generations) rat model that spontaneously expresses diabetes in all fa/fa males fed a standard rodent diet Purina 5008. In ZDF fa-fa males hyperglycemia begins to develop at about seven weeks of age and glucose levels (fed) typically reach 500 mg/DL by 10 to 11 weeks of age. Insulin levels (fed) are high during the development of diabetes. However, by 19 weeks of age insulin drops to about the level of lean control litter mates. Triglyceride and cholesterol levels of obese rats are normally higher than those of leans.

In the present experiment, three groups of 7-week old ZDF rats, with 6 rats per group, received the infusion treatment by ALZA pump for 14 days: 1) vehicle control, 2) and 3), PYY with two different doses, 100 pmol/kg/hr and 500 pmol/kg/hr respectively. Four measurements were taken before the infusion and after the infusion at day 7 and day 14: 1) plasma glucose level, 2) plasma insulin level, and 3) plasma triglycerides (TG) level, as well as oral glucose tolerance (OGTT) test.

Human, synthetic PYY was purchased from Sigma, and was re-suspended into 0.15 M NaCl with 0.5% BSA. The thee solutions thus comprised vehicle (0.15 M NaCl with 0.5% BSA), PYY 100 pmol/kg/hr, and PYY 500 pmol/kg/hr.

Figure 11 shows how the plasma glucose level (fed) was reduced over period of 14 days test in PYY-treated groups. The mean fed-plasma glucose level decreases over two weeks in PYY treated groups: it fell 40 mg/dl in the group receiving 100 pmol PYY and fell 82 mg/dl in the group receiving 500 pmol PYY. By contrast, it rose 11 mg/dl in the vehicle group. The data were plotted as percentage of the glucose level on day 0. These changes are statistically significant over time (P value = 0.05). It is well documented that the fed plasma glucose level increases in ZDF rats to between 300 and 350 mg/dl as they develop of diabetes from 7 to 9 weeks. The fact that the plasma glucose level dropped to 27% at 9 weeks of age in PYY treated groups suggests that PYY may have an effect on regulating fed plasma glucose level.

Figure 12 demonstrates how the plasma insulin level (fed) was preserved over period of 14 days test in PYY treated groups. The plasma insulin levels in the control group dropped from 17.5 +/- 0.9 to 9.1 +/- 1.3 ng/ml, whereas the insulin level was preserved in the PYY treated groups: it went from 18.2 +/- 3.6 to 15.1 +/- 1.8 ng/ml in the group receiving 100 pmol PYY, went from 18.6 +/- 1.2 to 17.3 +/- 3.6 ng/ml in the group receiving 500 pmol PYY. Fed plasma

insulin levels normally begin to decrease and eventually reach 1-5 ng/ml in these ZDF rats during as they develop diabetes from 7 week to post 9 weeks. The fact that plasma insulin level was preserved in PYY treated groups, but not in control groups, suggests that PYY may have an effect on β cell insulin release in response to high plasma glucose level in these pre-diabetic rats.

Figure 13 illustrates how glucose tolerance was improved in an OGTT test in PYY treated groups after 7 days of infusion. The rate of recovering to normal fasting glucose level in PYY treated groups (with 100 pmol/kg/hr) is significantly higher than that of the vehicle group during the last 60 to 120 min of the OGTT test (P value = 0.0024).

Figure 14 depicts how fasting plasma insulin level was higher in PYY treated groups after 14 days of the infusion. Fasting plasma insulin level of the rats treated with PYY was greater than the vehicle control. This is consistent with the observation in fed insulin level showing here in Figure 12. Again, it suggested that PYY might affect β cell insulin release in respond to the plasma glucose level.

The preliminary *in vivo* data suggest that PYY may affect on 1) regulation of insulin release by β cells in response to plasma glucose level, 2) control of the fed plasma glucose level and 3) improvement of glucose tolerance in 7- 9 week old pre-diabetic rats.

All of the above-cited references and publications are incorporated herein by reference.

Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

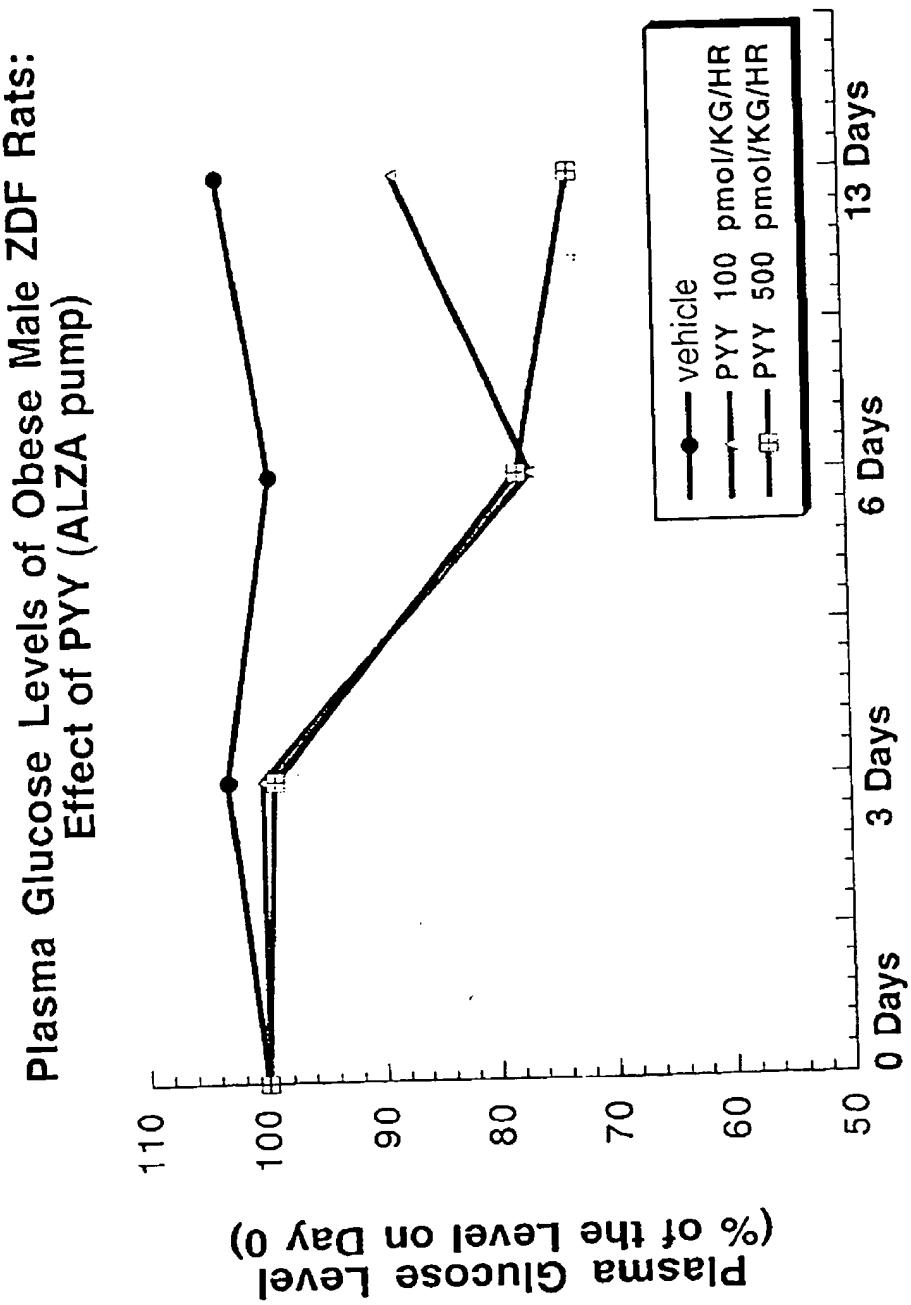

Fig 11

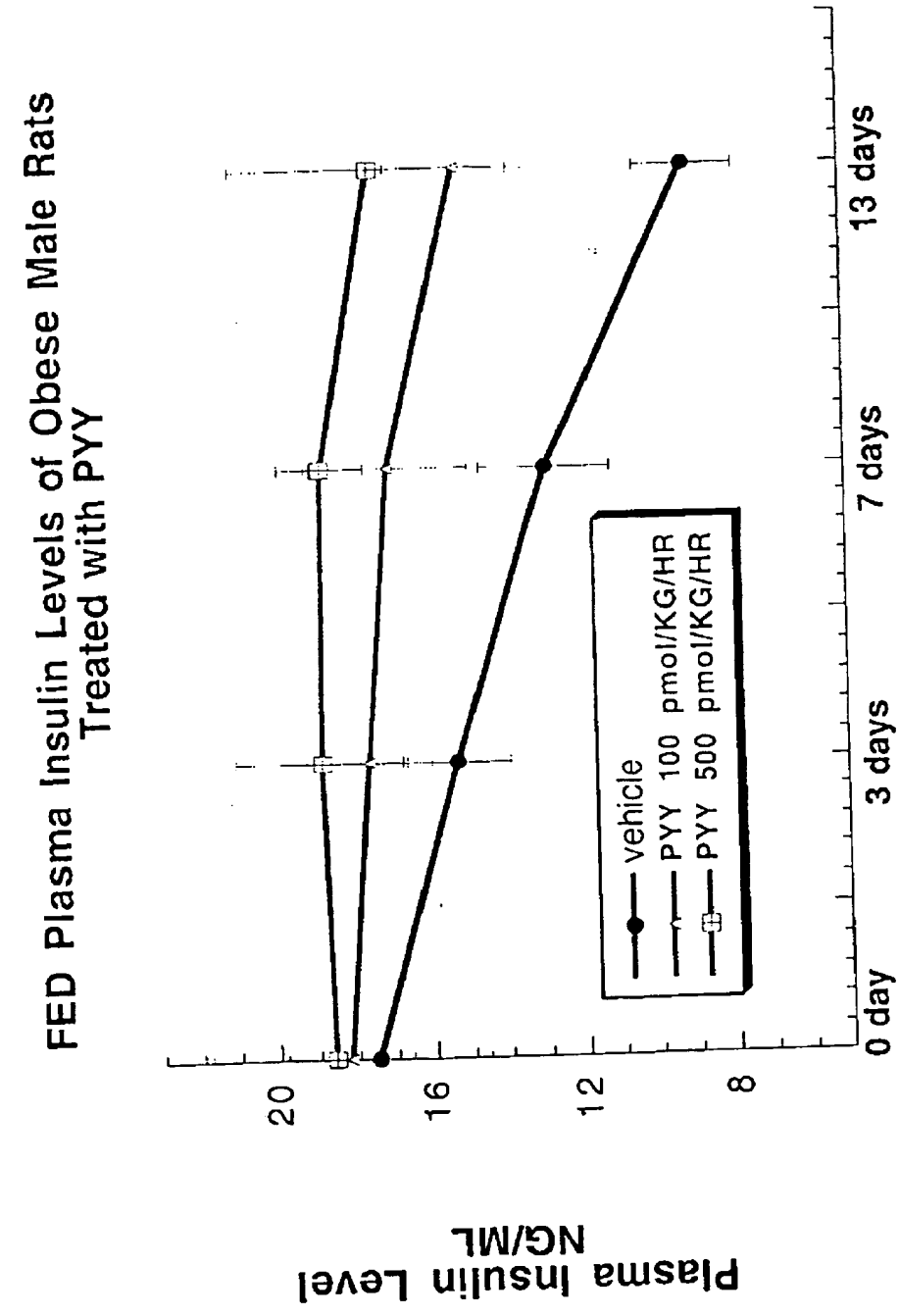

Fig 2

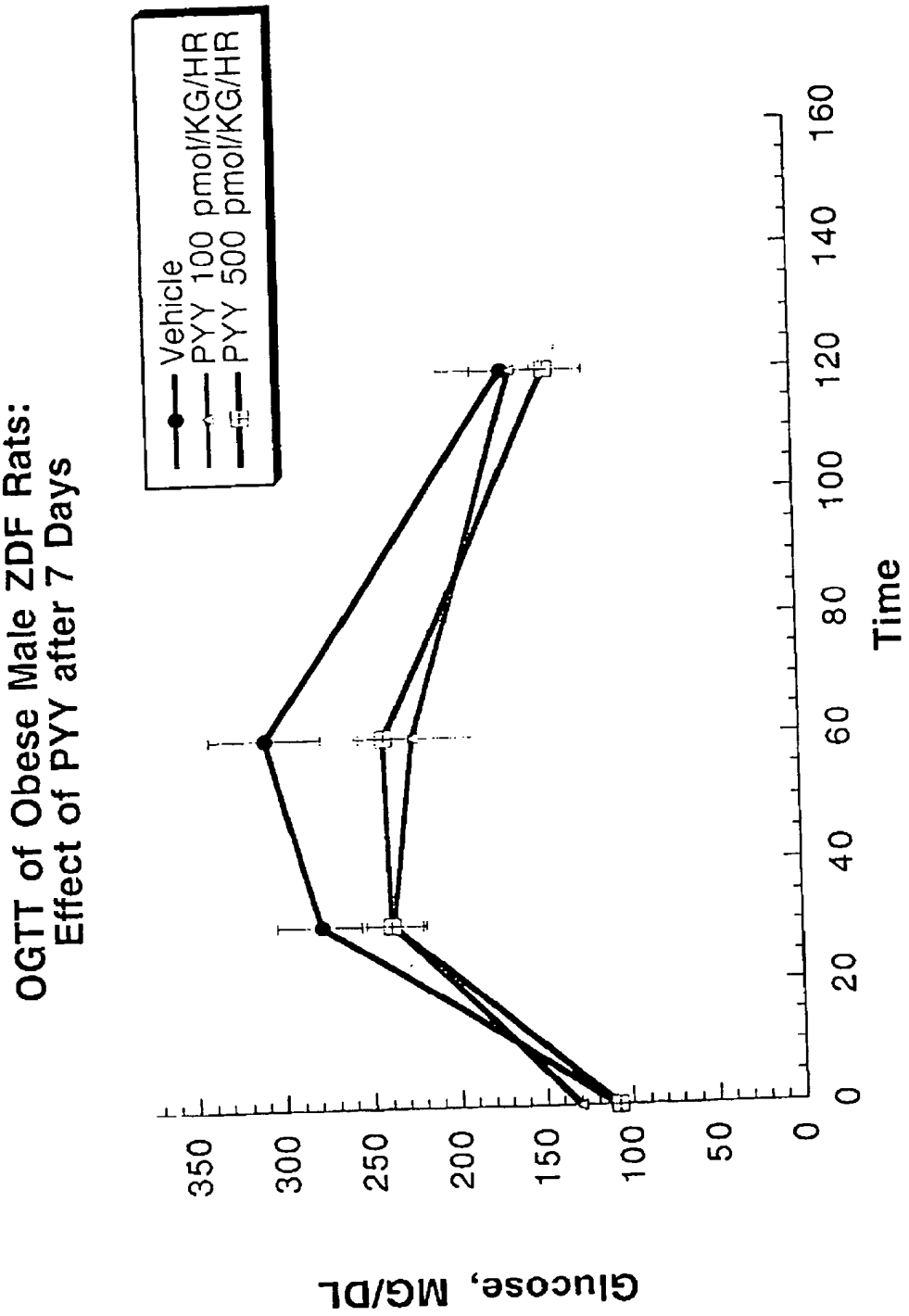

Fig 13

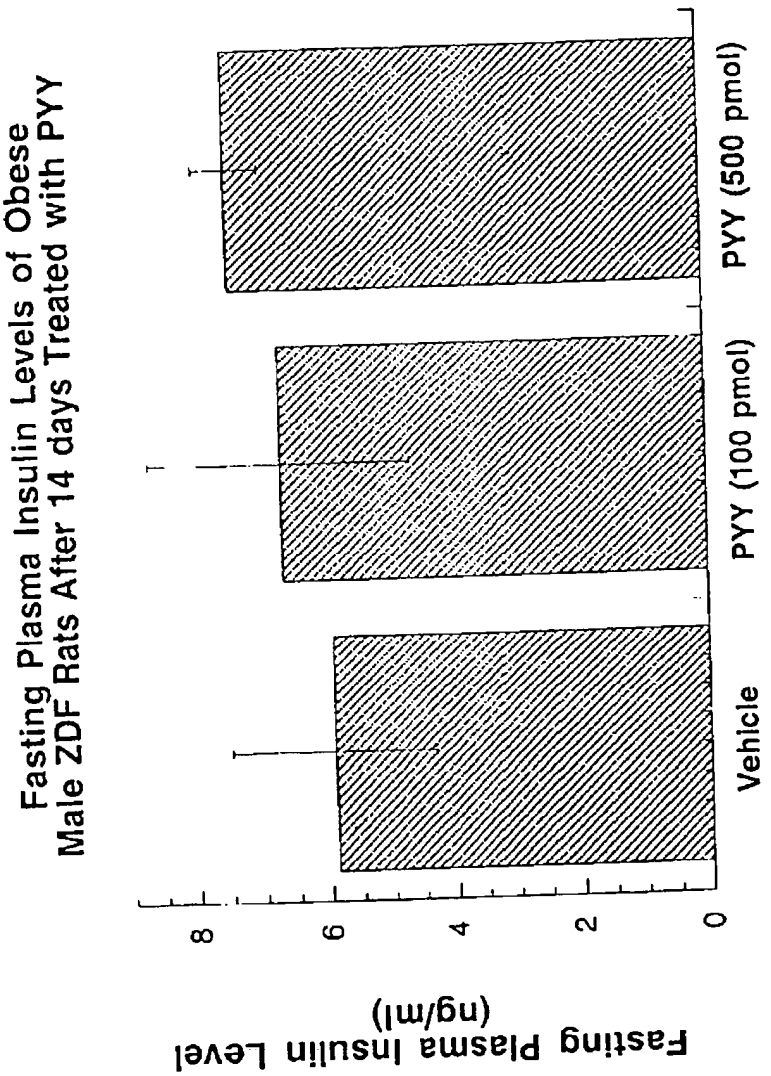

Fig. 14